

IN THE SPECIFICATION

At page 5, after line 1, insert the following paragraph:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee.

At page 5, at line 20 to page 6, line 1, replace with the following paragraph:

FIGS. 2A to 2G. Chromosomal instability in hSecurin^{+/+} cells. FISH analysis of hSecurin^{+/+} (FIG. 2A) and hSecurin^{-/-} cells (FIGS. 2B-E) with probes specific for chromosome 7 (red) and chromosome 12 (green) (FIGS. 2A-D), or with a pan-centromeric probe (FIG. 2E). Nuclear DNA was stained with DAPI (blue). (FIG. 2F) Chromosome gains and losses in hSecurin^{+/+} and hSecurin^{-/-} cells. The number of FISH signals per cell was determined for chromosomes 7, 12, 17, and X. The fraction of cells with FISH signals equal to the modal value of two (chromosomes 7, 12, and 17) or the modal value of one (X chromosome) is highlighted in yellowcross-hatched. Non-modal cell populations accounting for 5 percent or more of the total are highlighted in greendiagonal-hatched (for chromosome gains) and redvertical-hatched (for chromosome losses). The total fraction of cells off the mode is given in the far-right column, summary column. Summary of the percentage of hSecurin^{+/+} (HCT116) and hSecurin^{-/-} (KO1, KO2) cells off the mode (FIG. 2G, left top panel) and frequency of nuclear 'bud' structures in hSecurin^{+/+} and hSecurin^{-/-} cells (FIG. 2G, right bottom panel).

At page 6, line 13, replace with the following paragraph:

FIGS. 3A to 3D. Multiplex-FISH analysis of CIN phenotype in hSecurin^{-/-} cells.

FIG. 3A. M-FISH karyotype from a hSecurin^{-/-} cell metaphase.

FIGS. 3B-D. Summary of M-FISH data from parental hSecurin^{+/+} HCT116 cells (B) and

from hSecurin^{-/-} cells (C-D). Loss of a single copy of a given chromosome is marked in red vertical-hatched, loss of both copies is marked in black stippled, and gain of a single copy is marked in green diagonal-hatched.

At page 7, line 23 to page 8, line 1, replace with the following paragraph:

FIGS. 6B-6C. Separin immunoprecipitates were incubated with mitotic Xenopus extracts, washed, and added to purified cohesin complexes. Samples were taken at different time points and analyzed by immunoblotting with myc antibodies. Full-length SCC1-myc migrates at 18 150 kDa; a SCC1-myc cleavage product of 110 kDa (FIG. 7B~~6B~~B). A 55 kDa Scc1 cleavage product (arrows) absent from reactions using separin isolated from hSecurin-deficient cells (FIG. 7C~~6C~~C).